EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Sarclisa 100mg/5ml
Sarclisa 500mg/25ml

Date: March 2024

Unit: Technical Assessment Unit

Assessment report

Sarclisa

Administrative information:

Trade name of the medicinal product:	Sarclisa
INN (or common name) of the active substance(s):	Isatuximab100 mg/5ml Isatuximab 500 mg/25ml
Manufacturer of the finished product	Sanofi Aventis Deutschland GmbH; industriepark Hochst bruningstrabe 50, D-65926 Frankfurt am Main; Germany
Marketing Authorization holder	Sanofi Winthrop Industrie, 82 Avenue Raspail, 94250 Gentillty - France
Applied Indication(s):	SARCLISA is indicated: - in combination with pomalidomide and dexamethasone, for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy. - in combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy
Pharmaceutical form(s) and strength(s):	• Concentrate for solution for Infusion, colourless to slightly yellow solution. • Strength: Isatuximab100 mg/5ml and Isatuximab 500 mg/25ml.
Route of administration	Both concentrations are intended for intravenous use.
Approved Packs	**Sarclisa 100mg/5ml:** Carton box containing one coloulrless clear glass type I vial of 5ml, closed with ETFE (copolymer of ethylene and tetrafluoroetylene) coated bromobutyl stopper, crimped with an aluminium seal with a grey flip-off button and insert leaflet. **Sarclisa 500 mg/25ml:** Carton box containing one coloulrless clear glass type I vial of 25ml, closed with ETFE (copolymer of ethylene and tetrafluoroetylene) coated bromobutyl stopper, crimped with an aluminium seal with a grey flip-off button and insert leaflet.

List of abbreviations

ADCC	antibody-dependent cell-mediated cytotoxicity
ADCP	antibody-dependent cellular phagocytosis
CD	cluster of differentiation
CDC	complement-dependent cytotoxicity
CTD	common technical document
DP	Drug Product
DS	Drug Substance
EMA	European Medicines Agency
IgG1	immunoglobulin G1
WFI	Water of injections

Dossier initial submission and evaluation process:

- The product was submitted for registration via reliance model level I.
- The dossier was submitted to the registration administration units on 12.3.2023 when the applicant provided all the reliance required documents.
- Full (unredacted) EMA assessment report, List of questions at 120 day and 180 day and complete CTD of the product were provided.

1. General introduction about the product including brief description of the AI, its mode of action and indications.

- Sarclisa is presented as a concentrate for solution for infusion containing 20 mg/mL of Isatuximab as active substance. Other ingredients are: histidine, histidine hydrochloride monohydrate, sucrose, polysorbate 80 and water for injections (WFI) , No novel excipients were used.

-Sarclisa finished product is available in 2 single-use vial presentations: 500 mg/25 mL and 100 mg/5 mL.

- Isatuximab is a chimeric IgG1 derived-monoclonal antibody binding selectively the human CD38 **membrane protein** is composed of two kappa light chains each with molecular weight of approximately 23 kDa and two IgG1 heavy chains each with a molecular weight of approximately 49 kDa (deglycosylated form) linked through disulfide bridges.

-Isatuximab acts through IgG Fc-dependent mechanisms including antibody-dependent cell-mediated cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), and complement-dependent cytotoxicity (CDC). Isatuximab can also trigger tumor cell death by induction of apoptosis via an Fc-independent mechanism.

- In combination with pomalidomide and dexamethasone, for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy.

- In combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

2. **Quality aspects:**

- **Manufacturer**

-Isatuximab Drug substance was manufactured at Sanofi Chimie,9, quai Jules Guesde, BP35,94403 Vitry-sur-Seine cedex – FRANCE
-Sarclisa Finished product was manufactured at Sanofi aventis Deutschland GmbH; industriepark Hochst bruningstrabe 50, D-65926 Frankfurt am Main - Germany
-Manufacturing of both DS and DP are performed in accordance with current GMP regulations.

- **Stability**

Drug Substance

-Suggested Storage Conditions of the active substance: -30 ± 5 ℃.
-Suggested shelf life for the active substance: 36 months

Drug Product

-The finished product is Stored in a refrigerator (2°C–8°C). Do not freeze.
- Required shelf life for the drug product is 36 months
-Store in the original package in order to protect from light.

3.**Preclinical and clinical aspects:**

Overall, the primary preclinical studies provided adequate evidence that isatuximab alone or in combination with pomalidomide is capable of inducing anti-tumour effect on CD38 expressing Multiple myeloma.
In addition, The clinical benefit of adding isatuximab to pomalidomide and dexamethasone is demonstrated in relapsed and refractory multiple myeloma patients who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

General Conclusion and Recommendations if any:

Based on CTD module during registration, the product is approved

For more information, please visit EMA published assessment report link:
https://www.ema.europa.eu/en/documents/assessment-report/sarclisa-epar-public-assessment-report_en-0.pdf